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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,117	04/12/2001	Craig A. Rosen	6832.0015-00	6455

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EXAMINER	
ROBINSON, HOPE A	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/833,117	ROSEN ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) *22-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-11 and 13-21* is/are rejected.

7)☐ Claim(s) *12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response to the Office Action mailed November 4, 2003 on March 4, 2004 is acknowledged.

Claim Disposition

2. Claims 1-12 and 26 have been amended. Claims 1-59 are pending. Claims 1-21 (pertaining to interferon beta) are under examination.

3. The following grounds of rejection are or remain applicable:

Restriction Requirement

4. The response filed on March 2004, at page 17 requested clarification of the restriction requirement concerning the election made of a specific therapeutic protein X. The following inventions were found in the instant application:

Group I Claims 1-21 drawn to an albumin fusion protein comprising a therapeutic protein X (SEQ ID NO:) and albumin (SEQ ID NO:18), classified in class 424, subclass 192.1.

Group II Claims 22-25, drawn to a method of treating a disease or disorder in a patient, classified in class 514, subclass 12.

Group III Claim 26, drawn to a method of extending the shelf life of Therapeutic protein X (SEQ ID NO:), classified in class 435, subclass 449.

Group IV Claims 27-29, drawn to a nucleic acid molecule, classified in class 536, subclass 23.4.

Group V Claims 30-50 and 59, drawn to an albumin fusion protein comprising IL-2, classified in class 424, subclass 192.1.

Group VI Claims 51-54, drawn to a method of treating a disease or disorder in a patient using the fusion protein comprising IL-2, classified in class 514, subclass 12.

Group VII Claim 55, drawn to a method of extending the shelf life of IL-2, classified in class 435, subclass 449.

Group VIII Claims 56-58, drawn to a nucleic acid molecule encoding an albumin fusion protein comprising IL-2, classified in class 536, subclass 23.4.

The notation of: "therapeutic protein X (SEQ ID NO:)", meant that applicant needed to elect the sequence desired to be fused to SEQ ID NO:18 (Albumin). For clarification: Inventions I and III above need a further election of the specific Therapeutic X for examination which is not to be construed as a species election (therapeutic protein X (SEQ ID NO:), as the Table of Therapeutic protein X in the specification (Table 1) has several products that have different function, structure and modes of operation.

Applicant elected Group I, claims 1-21 on September 14, 2003 with traverse and the traversal was addressed in the office action mailed on November 4, 2003. Applicant has made a further election of a specific therapeutic protein X, interferon beta in the

amendment filed March 4, 2004 from Table 1 without traverse, which is examined in the office action below. Applicant's comments regarding a rejoinder of claims are noted.

5. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the

above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Information Disclosure Statement

6. The information disclosure statement filed on March 4, 2004 has been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 1-4, 13-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and the dependent claims hereto are indefinite for the recitation of "...wherein said fragment the ability to prolong the shelf life of interferon beta protein..." (see item b of claim 1), as it appears the word "has" is missing from the claim (see for example item c).

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

9. Claims 1-3, 5-10, 13-14 and 17-21 are rejected under 35 U.S.C. 103 (a) as being unpatentable over DELTA BIOTECHNOLOGY LTD. (WO 97/24445, July 10, 1997 or KR99076789, October 15, 1999) in view of CETUS CORPORATION (EP 215,658, September 12, 1986).

DELTA BIOTECHNOLOGY LTD. disclose serum albumin fusion proteins comprising the sequence set forth in SEQ ID NO: 18 of the instant application with a 100% sequence identity (claim 1, see the sequence alignment and page 1 of the reference). Additionally, the reference discloses that the albumin is useful as a component of a fusion protein because it is a stabilizer and transporter of other proteins (page 1) and that the fusion proteins have an increased circulatory half-life (shelf life) over unfused proteins (claim 2, page 3). The fusion protein of the claimed invention comprises "therapeutic protein X and albumin and the disclosure on page 2 indicates that the therapeutic protein is a polypeptide, antibody, peptide, fragments or variants thereof. DELTA BIOTECHNOLOGY LTD. discloses that the half-life (shelf-life) of the fusion protein is greater than the half-life of fusion partner by itself. Additionally, the reference teaches that activity assays showed that the conjugate retained full, and possibly increased activity *in vitro* ((claim 3, page 3). It is disclosed that fusion to the polypeptide is achieved by genetic manipulation such that the DNA coding for HSA or a fragment thereof is joined to the DNA coding for said polypeptide (claim 5 and page 2 of the instant specification, page 1 of the reference). The reference discloses fragments/variants thereof of SEQ ID NO: 18 (claim 6, page 3). Regarding claims 7, 8, 9 and 10 which depend from claims 5 and 6, however encompass the limitation that a portion of albumin is sufficient to prolong the shelf-life (half-life), these claims are also obvious over the reference which discloses the limitation of claims 5 and 6 and teach

biologically active fragments of albumin having the activity of increasing the half-live (page 3).

DELTA BIOTECHNOLOGY LTD. discloses fusion proteins that are non-glycosylated (claim 13, page 2). The reference also discloses expression in *S. cerevisiae* (yeast) as recited in claim 14 (pages 2, 4). It is also stated that expression can occur in animal cells in culture (claims 17-18, page 8). The reference discloses a leader sequence (claim 19, page 17). A composition comprising the albumin fusion protein coupled with an acceptable carrier is disclosed (claim 20, page 12). Regarding claim 21 and the recitation of a kit comprising the composition, the reference teaches a pharmaceutical formulation comprising the fusion protein with one or more acceptable carrier presented in a unit dosage form which is equivalent to a kit (page 12). Therefore, as the structure of the protein in the reference is identical to that of the instant application and the reference discloses albumin fusion proteins and fragments thereof with increased albumin activity, the claimed invention is obvious. In-so-far-as DELTA BIOTECHNOLOGY LTD. does not disclose an interferon beta protein, CETUS CORPORATION teach the use of albumin to stabilize interferon beta.

Therefore, it would have been obvious to one having ordinary skill in the art to make an albumin fusion protein because DELTA BIOTECHNOLOGY LTD. teach albumin fusion proteins and state that albumin is a useful component of a fusion protein because it is a stabilizer and transporter of other proteins (page 1) and that the fusion proteins have an increased circulatory half-life (shelf-life) over unfused proteins. One of ordinary skill in the art would be motivated to combine the teachings of the references to fuse interferon beta with albumin to make an albumin fusion protein because CETUS

CORPORATION teach a composition wherein interferon beta is stabilized by albumin. Moreover, CETUS CORPORATION teach that native beta-interferons are not lipophilic proteins, therefore, they can be stabilized by adding a stabilizer such as albumin and albumin is an art recognized stabilizer of interferons in aqueous solutions. In addition, DELTA BIOTECHNOLOGY LTD. teach that albumin can be fused to therapeutic protein X wherein the therapeutic protein can be a polypeptide, antibody, peptide, fragments or variants thereof and that prolonged shelf-life is a benefit to having the protein in a fused state. Therefore, the claimed invention was within the ordinary skill in the art to make and use at the time of filing, thus, *prima facie* obvious.

10. Applicant's arguments filed on March 4, 2004 have been fully considered. Note that new grounds of rejections have been implemented based on applicant's amendments to the claims under 35 U.S.C. 112, second paragraph and 103(a). The response on page 19 state that the reference cited by DELTA BIOTECHNOLOGY LTD. under 35 U.S.C. 102(b) does not teach or suggest an albumin fusion protein comprising an interferon beta protein. Note that this reference of record has been applied under 35 U.S.C. 103(a) for the reasons stated above. Applicant's statements regarding the rejection under 35 U.S.C. 102(b) is moot as the rejection has been withdrawn. However, as it applies to the newly instituted rejection under 35 U.S.C. 103(a) it will be addressed. The reference cited by DELTA BIOTECHNOLOGY LTD. is applicable to the claimed invention as an albumin fusion protein is taught and benefits to making such a fusion with albumin is also disclosed. The reference also provides guidance as to what types

of fusion partner albumin can have such as a polypeptide, antibody, peptide or fragments thereof. This reference is combined with a reference by CETUS CORPORATION, that teaches the use of albumin to stabilize interferon beta. The references are to be considered in combination not singly, and as stated above, the combined teachings of the references renders the claimed invention as obvious.

Conclusion

11. Claim 12 is objected to as the claim depends from a rejected based claim. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 9:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope A. Robinson, MS

Patent Examiner

SUPERVISORY PATENT EXAMINER
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